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Schiff base-Poloxamer P85 combination demonstrates chemotherapeutic effect on prostate cancer cells *in vitro*

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ABSTRACT

Prostate cancer is a multistep and complicated cancer type that is regulated by androgens at the cellular level and remains the second commonest cause of death among men. Discovery and development of novel chemotherapeutic agents enabling rapid tumor cell death with minimal toxic effects to healthy tissues might greatly improve the safety of chemotherapy.

The present study evaluates the anti-cancer activity of a novel heterodinuclear copper(II)Mn(II) complex (Schiff base) in combination with poly(ethylene oxide) and poly(propylene oxide) block copolymer (Pluronic) P85. We used assays for cell proliferation, apoptosis, cell migration and invasion, DNA binding and cleavage to elucidate the molecular mechanisms of action, in addition to the anti-inflammatory potency of the new combination. The combined treatment of Schiff base and P85 lead to a remarkable anti-cancer effect on prostate cancer cell lines. Cell proliferation was inhibited in Schiff base-P85 treatment. The activity of this formulation is on DNA binding and cleavage and prevents inflammation in *in vitro* conditions. This is the first study presenting the anti-cancer activity of the present Schiff base derivative and its combination with P85 to treat prostate cancer *in vitro*.

1. Introduction

Prostate cancer is a multistep and complicated cancer type which is characterized by hormone regulation at the molecular and cellular level, and is the most common cancer with a high prevalence [1,2]. Although androgen deprivation therapy is used as a first line treatment option for several years, a concomitant chemotherapeutic treatment is often required for a successful treatment outcome [3]. Therefore, the improvement of current therapeutic approaches, screening of new drugs and identification of new agents is essential for the treatment of advanced prostate cancer. The introduction of many novel targeted therapeutics into clinical practice is a rapidly growing field in medical oncology. Cancer chemotherapy involves targeting cancer cells with cytotoxic agents. Chemotherapy has been considered as a solution for the treatment of many cancers, resulting in destruction of malignant cells, while having a nonspecific toxicity on all other cell types. The current chemotherapeutic approach for prostate cancer is to use single or combined chemotherapeutic agents to increase survival rates for hormone refractory disease [4]. These therapeutic strategies are able to devastate the tumor but are often ineffective on advanced prostate cancer. Although the combination of the chemotherapeutic agents is considered to be effective against prostate cancer, there is currently no reported data regarding the increased survival rates or improved patients life quality [5]. Developments of new chemotherapeutic agents that enable the inhibition of prostate cancer progression are the aim of interest. Moreover, the impact of cytotoxic chemotherapy is not limited to the cancer tissue. Therefore, future treatments will include cytotoxic tools that preferentially target tumor cells.

Pluronics as an interesting class of polymeric materials arranged in a triblock structure consisting of poly(ethylene oxide) (PEO) and poly(propylene oxide) (PPO) units. The number of these hydrophilic and hydrophobic units determines the micelle characteristics and diameter of micelles carrying drug molecules

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